

Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Currently Amended) Method for detecting disease-associated autoantibodies, which are directed at G protein-coupled receptors for diagnosis of autoimmune diseases, comprising characterized in that ~~the method comprises the following steps:~~
 - a) Bringing bodily fluid into contact with ~~a denaturing agent~~ an agent for precipitating autoantibodies, wherein a fraction of said fluid comprising said autoantibodies is precipitated,
 - b) Bringing the precipitated fraction into contact with a peptide, ~~particularly one comprising Biotin which comprises a sequence or partial sequence of the first and/or second loop of the~~ a G protein-coupled receptor and a tag, whereby a mixture is formed in which the autoantibodies bind said sequence or partial sequence of said peptide,
 - c) Incubating the mixture with a carrier coated with ~~avidin or streptavidin~~ an anti-tag to bind said tag,
 - d) Washing ~~the materials of~~ the carrier,
 - e) Incubating the carrier with anti-IgG antibody subclasses, ~~whereby wherein~~ the anti-IgG antibody is marked for an enzyme reaction or color reaction, and
 - f) Carrying out ~~an said~~ enzyme reaction or color reaction to detect disease-associated autoantibodies, which are directed at said G protein-coupled receptor to diagnose said diseases.
2. (Currently Amended) Method of claim 1, ~~characterized in that~~ wherein the ~~denaturing agent~~ for precipitating autoantibodies is ammonium sulfate and/or alcohol.
3. (Currently Amended) Method of claim 1, ~~characterized in that~~ wherein the carrier is a magnetic particle or an ELISA plate.
4. (Currently Amended) Method of claim 1,
Appl. No. 10/536,552
Page 4

~~characterized in that wherein~~

the autoantibodies are directed against a beta1-adrenergic receptor, a muscarinic M2 receptor, an angiotensin II AT1 receptor, an alpha1-adrenergic receptor, and an endothelin IA receptor, a PAR-1, PAR-2, and/or PAR-3.

5. (Currently Amended) Method of ~~Claims 4~~ claim 4,

~~characterized in that wherein~~

the autoantibodies directed against the beta1-adrenergic receptor are associated with dilatative cardiomyopathy, Chagas' myocardiopathy, or myocarditis; the autoantibodies directed against the muscarinic M2 receptor are associated with dilatative cardiomyopathy and/or Chagas' cardiomyopathy; the autoantibodies directed against the angiotensin II AT1 receptor are associated with preeclampsia, and/or malignant hypertension; the autoantibodies directed against the alpha1-adrenergic receptor are associated with essential hypertension, refractory hypertension, pulmonary hypertension and/or psoriasis; and/or the autoantibodies directed against endothelin IA receptor, PAR-1, PAR-2 and/or PAR-3 are associated with Raynaud's syndrome.

6. (Currently Amended) Method of claim 1,

~~characterized in that wherein~~

the peptide that comprises a sequence or partial sequence of the first and/or second loop of the receptor is used in the detection of autoantibodies associated with dilatative cardiomyopathy myocardiopathy, myocarditis, essential hypertension, refractory hypertension, pulmonary hypertension, or psoriasis, and that the peptide that comprises a sequence or partial sequence of the second loop of the receptor is used for Chagas' myocardiopathy, dilatative myocardiopathy cardiomyopathy, and/or Raynaud' s syndrome.

7. (Currently Amended) Method of claim 1,

~~characterized in that wherein~~

- the autoantibodies associated with dilatative cardiomyopathy are brought into contact with the peptide comprising a sequence or partial sequence of the first and/or second loop of the beta1-adrenergic receptor,
- the autoantibodies associated with Chagas' cardiomyopathy are brought into contact with the peptide comprising a sequence or partial sequence of the second loop of the beta1-

- adrenergen receptor,
- the autoantibodies associated with myocarditis are brought into contact with the peptide comprising a sequence or partial sequence of the first and/or second loop of the beta1-adrenergen receptor,
 - the autoantibodies associated with dilatative cardiomyopathy are brought into contact with the peptide comprising a sequence or partial sequence of the second loop of the muscarinergen M2 receptor,
 - the autoantibodies associated with Chagas' cardiomyopathy are brought into contact with the peptide comprising a sequence or partial sequence of the second loop of the muscarinergen M2 receptor,
 - the autoantibodies associated with preeclampsia are brought into contact with the peptide comprising a sequence or partial sequence of the second loop of the angiotensin II AT1 receptor,
 - the autoantibodies associated with malignant hypertension are brought into contact with the peptide comprising a sequence or partial sequence of the second loop of the angiotensin II AT1 receptor,
 - the autoantibodies associated with essential hypertension are brought into contact with the peptide comprising a sequence or partial sequence of the first and/or second loop of the alpha1-adrenergen receptor,
 - the autoantibodies associated with refractory hypertension are brought into contact with the peptide comprising a sequence or partial sequence of the first and/or second loop of the alpha1-adrenergen receptor,
 - the autoantibodies associated with pulmonary hypertension are brought into contact with the peptide comprising a sequence or partial sequence of the first and/or second loop of the alpha1-adrenergen receptor,
 - the autoantibodies associated with psoriasis are brought into contact with the peptide comprising a sequence or partial sequence of the first and/or second loop of the alpha1-adrenergen receptor,
 - the autoantibodies associated with Raynaud' s Syndrome are brought into contact with the peptide comprising a sequence or partial sequence of the first and/or second loop of the endothelin IA receptor, PAR-1, PAR-2 and/or PAR-3.

characterized in that
the IgG subclasses are IgG1, IgG2, IgG3 and/or IgG4 subclasses wherein the tag is biotin and
the anti-tag is avidin or streptavidin.

9. (Currently Amended) Method of claim 1,
characterized in that wherein

- in the case of dilatative cardiomyopathy, the IgG3 and/or IgG4 subclasses are used are detected if the peptide comprises a sequence or partial sequence of the first loop, and/or the IgG1 subclass is used is detected if the peptide comprises a sequence or partial sequence of the second loop,
- in the case of Chagas' cardiomyopathy, the IgG1, IgG2, IgG3 and/or IgG4 subclasses are used is detected,
- in the case of myocarditis, the IgG3 and/or IgG4 subclasses are used are detected if the peptide comprises a sequence or partial sequence of the first loop, and/or the IgG1 subclass is used is detected if the peptide comprises a sequence or partial sequence of the second loop,
- in the case of preeclampsia, the IgG3 subclass is used is detected,
- in the case of malignant hypertension, the IgG1 and/or IgG3 subclasses are used are detected,
- in the case of essential hypertension, the IgG1 and/or IgG3 subclasses are used are detected if the peptide comprises a sequence or partial sequence of the first loop, and/or the IgG2 subclass is used is detected if the peptide comprises a sequence or partial sequence of the second loop,
- in the case of refractory hypertension, the IgG1 and/or IgG3 subclasses are used are detected if the peptide comprises a sequence or partial sequence of the first loop, and/or the IgG2 subclass is used is detected if the peptide comprises a sequence or partial sequence of the second loop,
- in the case of pulmonary hypertension, the IgG1, IgG2, IgG3 and/or IgG4 subclasses are used are detected, in the case of psoriasis, the IgG1, IgG2, IgG3 and/or IgG4 subclasses are used are detected, and/or
- in the case of Raynaud's Syndrome, the IgG1 subclass is used is detected.

10. (Currently Amended) Method of claim 1,

characterized in that wherein the autoantibodies are concentrated or purified before being

Appl. No. 10/536,552

Page 7

detected-identified.

11. (Currently Amended) Method of claim 10,
~~characterized in that wherein~~
the method for concentrating or purifying the autoantibodies comprises the following steps:
a) i) Obtaining an IgG fraction from bodily fluid,
b) ii) Bringing the IgG fraction that was obtained into contact with a peptide that comprises a partial sequence of a first or second loop of a G protein-coupled receptor and a tag, whereby a mixture is obtained in which the autoantibody bind said partial sequence of said peptide,
e) iii) Incubating the mixture with a carrier coated with an anti-tag to bind said tag and that is washed and concentrated, and
d) iv) Eluting the autoantibodies from the concentrated carrier.
12. (Currently Amended) Method of claim 1,
~~characterized in that wherein~~
the ~~peptide that comprises the sequence or~~ partial sequence of the first and/or second loop is selected from the group ~~comprising consisting of~~ EYGSFF [SEQ ID NO: 1], SFFCEL [SEQ ID NO: 2], ARRCYND [SEQ ID NO: 3], PKCCDF [SEQ ID NO: 4], AESDE [SEQ ID NO: 5], CYIQFF [SEQ ID NO: 6], EDGE CY [SEQ ID NO: 7], VRTVEDGECYIQFFSNAAVTFGTAI [SEQ ID NO: 8], AFHYESQ [SEQ ID NO: 9], ENTNIT [SEQ ID NO: 10], FWA FGR [SEQ ID NO: 11], GRAFCDV [SEQ ID NO: 12], ITEEAGY [SEQ ID NO: 13], ERFCGI [SEQ ID NO: 14], GRIFCD [SEQ ID NO: 15] and/or ITTCHDVL [SEQ ID NO: 16].
13. (Cancelled)
14. (Cancelled)
15. (Currently Amended) Method of claim 1,
~~characterized in that wherein~~
the peptide is modified ~~by means of~~-deletion, addition, substitution, translocation, inversion and/or insertion- substitution.

16. (Withdrawn) Peptide selected from the group comprising EYGSFF, SFFCEL, ARRCYND, PKCCDF, AESDE, CYIQFF, EDGEY, VRTVEDGECYIQFFSNAAVTFGTAI, AFHYESQ, ENTNIT, FWAFFGR, GRAFCDV, ITEEAGY, ERFCGI, GRIFCD and/or ITTCHDVL, for use as a medicinal active substance.
17. (Withdrawn) Peptide of claim 16,
characterized in that
the peptide is bound by autoantibodies of patients having one of the following diseases: dilatative cardiomyopathy, Chagas' cardiomyopathy, myocarditis, preeclampsia, malignant hypertension, essential hypertension, refractory hypertension, pulmonary hypertension, psoriasis and/or Raynaud's Syndrome.
18. (Withdrawn) Peptide of claim 16,
characterized in that
the peptide is immobilized.
19. (Withdrawn) Peptide of claim 16,
characterized in that
the peptide the peptide is bound to a solid phase.
20. (Withdrawn) Recognition molecule directed against the peptide of claim 16.
21. (Withdrawn) Recognition molecule of claim 20,
characterized in that
it is an antibody, a lectin, an antisense construct, and/or a chelator.
22. (Withdrawn) Pharmaceutical composition comprising a peptide selected from the group comprising EYGSFF, SFFCEL, ARRCYND, PKCCDF, AESDE, CYIQFF, EDGEY, VRTVEDGECYIQFFSNAAVTFGTAI, AFHYESQ, ENTNH, FWAFFGR, GRAFCDV, ITEEAGY, ERFCGI, GRIFCD and/or ITTCHD
and/or a recognition molecule directed against the peptide.
23. (Withdrawn) Kit comprising a peptide selected from the group comprising

EYGSFF, SFFCEL, ARRCYND, PKCCDF, AESDE, CYIQFF, EDGEYC, VRTVEDGEYCIIQFFSNAAVTFGTAI, AFHYESQ, ENTNIT, FWAFFGR, GRAFCDV, ITEEAGY, ERFCGI, GRIFCD and/or ITTCHD, a recognition molecule directed against the peptide, and/or a pharmaceutical composition comprising the peptide and/or the recognition molecule, if applicable with Instructions for combining the contents of the kit and/or for making available a formulation.

24. (Withdrawn) Chromatography device comprising peptides selected from the group comprising EYGSFF, SFFCEL, ARRCYND, PKCCDF, AESDE, CYIQFF, EDGEYC, VRTVEDGEYCIIQFFSNAAVTFGTAI, AFHYESQ, ENTNIT, FWAFFGR, GRAFCDV, ITEEAGY, ERFCGI, GRIFCD and/or ITTCHD and/or recognition molecules directed against the peptide.
25. (Withdrawn) Device of claim 24, characterized in that the peptides are bound to the solid phase.
26. – 29. (canceled)
30. (Withdrawn) Method for treating an autoimmune disease, selected from the group comprising dilatative cardiomyopathy, Chagas' cardiomyopathy, myocarditis, preeclampsia, malignant hypertension, essential hypertension, refractory hypertension, pulmonary hypertension, psoriasis, Raynaud's syndrome, by means of binding and/or removing antibodies by means of peptides selected from the group comprising EYGSFF, SFFCEL, ARRCYND, PKCCDF, AESDE, CYIQFF, EDGEYC, VRTVEDGEYCIIQFFSNAAVTFGTAI, AFHYESQ, ENTNIT, FWAFFGR, GRAFCDV, ITEEAGY, ERFCGI, GRIFCD and/or ITTCHD, bound to a solid phase.
31. (Withdrawn) Method of claim 30, characterized in that the autoantibodies are directed against beta1-adrenergic receptors in the case of dilatative cardiomyopathy, against beta1-adrenergic receptors in the case of Chagas' cardiomyopathy, against beta1-adrenergic receptors in the case of myocarditis, against muscarinergic M2 receptors in the case of dilatative cardiomyopathy, against muscarinergic M2 receptors in the case of Chagas' cardiomyopathy, against angiotensin II AT1 receptors in the case of

preeclampsia, against angiotensin II AT1 receptors in the case of malignant hypertension, against alpha1-adrenergic receptors in the case of essential hypertension, against alpha1-adrenergic receptors in the case of refractory hypertension, against alpha1-adrenergic receptors in the case of pulmonary hypertension, against alpha1-adrenergic receptors in the case of psoriasis, and that the autoantibodies are directed against endothelin IA, PAR-1 PAR-2 and/or PAR-3 in the case of Raynaud's Syndrome.

32. (Currently Amended) Method for the ~~prophylaxis, diagnosis, therapy, monitoring the progression as well as follow-up treatment~~ of autoimmune diseases selected from the group comprising consisting of dilatative cardiomyopathy, Chagas' cardiomyopathy, myocarditis, preeclampsia, malignant hypertension, essential hypertension, refractory hypertension, pulmonary hypertension, psoriasis and Raynaud' s Syndrome, comprising the ~~step of using~~ providing one or more chosen from the following

(a) Peptide selected from the group

~~comprising~~ consisting of EYGSFF [SEQ ID NO: 1], SFFCEL [SEQ ID NO: 2], ARRCYND [SEQ ID NO: 3], PKCCDF [SEQ ID NO: 4], AESDE [SEQ ID NO: 5], CYIQFF [SEQ ID NO: 6], EDGEYC [SEQ ID NO: 7], VRTVEDGECYIQFFSNAAVTFGTAI [SEQ ID NO: 8], AFHYESQ [SEQ ID NO: 9], ENTNIT [SEQ ID NO: 10], FWAAGR [SEQ ID NO: 11], GRAFCDV [SEQ ID NO: 12], ITEEAGY [SEQ ID NO: 13], ERFCGI [SEQ ID NO: 14], GRIFCD [SEQ ID NO: 15] and/or ITCHDVL [SEQ ID NO: 16].

(b) a recognition molecule directed against said peptide,

(c) a pharmaceutical composition comprising said peptide and said recognition molecule, or

(d) a kit comprising one of said peptide, said recognition molecule or said pharmaceutical composition, optionally with instructions for combining the contents of the kit and/or for making available a formulation and

(e) a chromatography device comprising said peptide or said recognition molecule, and diagnosing or monitoring the progression of said autoimmune diseases.

33. (Withdrawn) Method for the production of a medication for the treatment of autoimmune diseases selected from the group comprising dilatative cardiomyopathy, Chagas' cardiomyopathy, myocarditis, preeclampsia, malignant hypertension, essential hypertension, refractory hypertension, pulmonary hypertension, psoriasis and/or Raynaud' s syndrome, comprising the step of using one or more chosen from the following (a) Peptide

selected from the group comprising EYGSFF, SFFCEL, ARRCYND, PKCCDF, AESDE, CYIQFF, EDGEY, VRTVEDGECYIQFFSNAAVTFGTAI, AFHYESQ, ENTNIT, FWAFFGR, GRAFCDV, ITEEAGY, ERFCGI, GRIFCD and ITTCHDVL (b) a recognition molecule directed against said peptide (c) a pharmaceutical composition comprising said peptide and said recognition molecule (d) a kit comprising one of said peptide, said recognition molecule or said pharmaceutical composition, optionally with instructions for combining the contents of the kit and/or for making available a formulation and (e) a chromatography device comprising said peptide or said recognition molecule.

34. (Withdrawn) Method for Screening medications, comprising the step of one or more chosen from the following (a) Peptide selected from the group comprising EYGSFF, SFFCEL, ARRCYND, PKCCDF, AESDE, CYIQFF, EDGEY, VRTVEDGECYIQFFSNAAVTFGTAI, AFHYESQ, ENTNIT, FWAFFGR, GRAFCDV, ITEEAGY, ERFCGI, GRIFCD and ITTCHDVL (b) a recognition molecule directed against said peptide (c) a pharmaceutical composition comprising said peptide and said recognition molecule (d) a kit comprising one of said peptide, said recognition molecule or said pharmaceutical composition, optionally with instructions for combining the contents of the kit and/or for making available a formulation and (e) a chromatography device comprising said peptide or said recognition molecule.

35. (Currently Amended) Method for detecting, ~~binding, complexing or neutralizing~~ of autoantibodies, directed against beta 1-adrenergic receptor, muscarinic M2 receptor, angiotensin II AT1 receptor, alpha1-adrenergic receptor, endothelin IA receptor, PAR-1, PAR-2, and/or PAR-3, comprising ~~the step of using~~

providing a peptide selected from the group comprising EYGSFF [SEQ ID NO: 1], SFFCEL [SEQ ID NO: 2], ARRCYND [SEQ ID NO: 3], PKCCDF [SEQ ID NO: 4], AESDE [SEQ ID NO: 5], CYIQFF [SEQ ID NO: 6], ~~EDGEY~~ EDGEY [SEQ ID NO: 7], VRTVEDGECYIQFFSNAAVTFGTAI [SEQ ID NO: 8], AFHYESQ [SEQ ID NO: 9], ENTNIT [SEQ ID NO: 10], FWAFFGR [SEQ ID NO: 11], GRAFCDV [SEQ ID NO: 12], ITEEAGY [SEQ ID NO: 13], ERFCGI [SEQ ID NO: 14], GRIFCD [SEQ ID NO: 15] and/or ITTCHDVL [SEQ ID NO: 16], and

detecting said autoantibodies.

36. (New) The method of claim 12, wherein the peptides are EYGSFF [SEQ ID NO: 1],

SFFCEL [SEQ ID NO: 2], ARRCYND [SEQ ID NO: 3] or PKCCDF [SEQ ID NO: 4].

37. (New) The method of claim 1, wherein the peptide comprises a partial sequence of the first and/or second loop of the G protein-coupled receptor and a tag.